

General

Guideline Title

Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association.

Bibliographic Source(s)

Johnson KA, Minoshima S, Bohnen NI, Donohoe KJ, Foster NL, Herscovitch P, Karlawish JH, Rowe CC, Carrillo MC, Hartley DM, Hedrick S, Pappas V, Thies WH. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. J Nucl Med. 2013 Mar;54(3):476-90. [80 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Appropriate Use Criteria

Amyloid imaging is appropriate in the situations listed below for individuals with all of the following characteristics:

Preamble: (i) a cognitive complaint with objectively confirmed impairment; (ii) Alzheimer's disease (AD) as a possible diagnosis, but when the diagnosis is uncertain after a comprehensive evaluation by a dementia expert; and (iii) when knowledge of the presence or absence of brain amyloid β (A β) pathology is expected to increase diagnostic certainty and alter management.

1. Patients with persistent or progressive unexplained mild cognitive impairment (MCI)
2. Patients satisfying core clinical criteria for possible AD because of unclear clinical presentation, either an atypical clinical course or an etiologically mixed presentation
3. Patients with progressive dementia and atypically early age of onset (usually defined as 65 years or less in age)

Amyloid imaging is inappropriate in the following situations:

4. Patients with core clinical criteria for probable AD with typical age of onset
5. To determine dementia severity
6. Based solely on a positive family history of dementia or presence of apolipoprotein E (APOE) ϵ 4
7. Patients with a cognitive complaint that is unconfirmed on clinical examination
8. In lieu of genotyping for suspected autosomal mutation carriers
9. In asymptomatic individuals

10. Nonmedical use (e.g., legal, insurance coverage, or employment screening)

Discussion of Individual Indications

Preamble

The Amyloid Imaging Taskforce (AIT) considered whether to specify the patient characteristics for each indication separately, but recognized that there were several elements common to all appropriate indications and set these elements apart in a separate preamble. The preamble was intended to characterize all patients for whom the appropriate indications 1 to 3 apply.

The preamble restricts substantially the set of patients for whom amyloid imaging would be appropriate in several ways. First, the dementia expert, as defined in the original guideline document, must evaluate the patient and determine that there is objective evidence of impairment. The objective evidence may be acquired and interpreted directly by the dementia expert in a detailed mental status examination or obtained from a separate neuropsychological assessment. Second, the expert should evaluate all available clinical evidence, including the history, physical and neurological examinations, and all available laboratory and neuroimaging data to consider the possible causes of the illness as well as potentially confounding circumstances such as depression, medication effects, and cerebrovascular, endocrine, or other medical disorders. This is because the presence of amyloid pathology in the brain, when considered in isolation, is insufficient to determine the cause of the impairment; rather, the presence of amyloid pathology is one factor among many that must be considered. The dementia expert must conclude on the basis of all available evidence that (i) the cause of the impairment is uncertain and (ii) that it could be explained on the basis of A β pathology (i.e., AD dementia or its prodromal stage must be in the differential diagnosis).

Last, the expert must conclude that a determination of either amyloid positivity or amyloid negativity would both increase the level of diagnostic certainty and alter the plan for patient management. Empirical evidence for the value of added certainty resulting from amyloid positron emission tomography (PET) has not yet been reported; however, several patient-centered outcome studies are underway, and the following should serve to guide efforts of this type further. The AIT considered several situations in which the added certainty of amyloid PET could be useful to patients and caregivers, and could result in altered management. First, many patients with uncertain diagnoses undergo extensive and repeated testing that would be reduced if the diagnostic certainty were increased by amyloid PET. For others, however, it is also likely that amyloid negativity would require additional diagnostic testing as the dementia expert seeks to identify the underlying A β -negative cause of impairment. The relative utility of diagnostic tests should be evaluated further. Second, increased certainty of the diagnosis could provide a basis for earlier and more consistent drug treatment, avoidance of treatments unlikely to afford benefit, and improved monitoring for likely complications and adverse drug effects that are relevant to specific dementing diseases. In addition, improved diagnostic certainty could provide more powerful motivation to make required lifestyle changes and difficult living transitions for which they are otherwise reluctant. Third, a more certain diagnosis can have profound social benefits to patients and families, who may need to identify the required resources and plan for future management. Minimizing diagnostic uncertainty can assist in bringing family members to a uniform understanding of the patient's condition and needs, facilitating the development of a unified plan of progressive support that best manages financial resources and maximizes quality of life.

Although learning the cause of dementia and the limited efficacy of available treatments may cause stress and anxiety for some, the AIT believes that the value of knowing outweighs the disadvantages. Electing to manage dementing diseases without investigating the cause or with high levels of diagnostic uncertainty often contributes to inconsistent and poor quality of care. In any circumstance, patients and their families decide—on their own—whether to seek answers by electing or failing to seek care.

Indication 1 (Appropriate): Patients with Persistent or Progressive Unexplained MCI

This indication refers to a patient who satisfies all the criteria set forth in the preamble and is being evaluated for persistent or progressive cognitive impairment that is still mild (e.g., a patient with MCI as defined in the original guideline document). This means, in practice, that although impaired according to objective measures, the patient does not have "significant interference in the ability to function at work or in usual daily activities." In this circumstance, an amyloid PET finding of positivity would, on the basis of its known correspondence to brain A β , raise the level of certainty that the patient's mild impairment is on the basis of AD pathology and represents early AD dementia (see the definitions in the original guideline document). However, it is important to emphasize again that not all patients with MCI would be appropriate for amyloid PET. Rather, amyloid PET would be appropriate only in those individuals who the dementia expert has concluded would benefit from greater certainty of the underlying pathology and whose clinical management would change as a result of this greater certainty.

The dementia expert should recognize that asymptomatic amyloid deposition is common in older (e.g., >75 years) individuals and may not be related to a patient's presenting symptoms. Furthermore, the dementia expert will need to consider in older individuals the possibility that amyloid positivity could be present but not the sole factor in causing the impairment and that comorbid conditions or pathologies such as vasculopathy could be present and could account for or significantly contribute to the observed impairment.

The prognostic value of amyloid PET for predicting future outcomes in MCI patients is under active investigation, and preliminary studies are

suggestive but not complete. Initial reports suggest that the majority of patients with amnesic MCI, variously defined by neuropsychological evaluation, and a positive amyloid PET will progress to AD dementia, whereas the risk of progression to AD dementia is significantly lower in those who are amyloid negative. The available evidence to date has not definitively linked amyloid positivity in individual patients with a future time point when cognitive or functional deterioration can be predicted. Therefore, currently the use of amyloid PET to predict the trajectory of a patient's cognitive decline or the time to any specific outcome is not appropriate because published evidence is limited (see the "Further Research Questions" section in the original guideline document).

A related, alternative scenario for this indication is a patient, also satisfying all the criteria set forth in the preamble, who is amyloid negative and therefore much less likely to be impaired on the basis of AD. The amyloid-negative scenario may, in practice, be the most frequently useful scenario in MCI, given the potential confound of age-associated A β , discussed earlier, among amyloid-positive individuals. Thus, in patients with MCI whose clinical picture may be complicated with potential vascular, traumatic, or medical causes of cognitive impairment, amyloid PET may find utility and could be used appropriately to exclude AD pathology effectively as a basis for the clinical syndrome.

Indication 2 (Appropriate): Patients Satisfying Core Clinical Criteria for Possible AD (i.e., Atypical Clinical Course or Etiologically Mixed Presentation)

This indication refers to a patient with an established dementia syndrome who is not typical with regard to presentation and clinical course, or to a patient who is considered to have a mixture of causal pathological processes. It is intended to explicitly exclude from the category of appropriate use the patient about whom there is little doubt of the underlying pathology because the onset, course, and examination findings are typical of AD dementia. It is, however, intended to include those patients for whom substantial uncertainty exists and for whom greater confidence would result from determining whether A β pathology is present or not present, as described next.

The AIT chose, here, to rely on the established concept of possible AD, specifically as it has been recently revised, and again to focus on the dementia specialist as the physician who would apply the criteria based on this diagnostic category. The restriction in this indication to patients with possible AD dementia is based on the well-established existence of patients about whom there is substantial doubt of whether the dementia is based on AD pathology. The sources of doubt are (i) the presence of an unusual course (e.g., sudden onset or episodic) or because the course cannot be established from the history or from retrospective cognitive test data, or (ii) the presence of a comorbid condition that confounds the interpretation of the clinical data, such as cerebrovascular disease, other neurological disease, other medical condition, or medication use that is affecting cognition and function. Amyloid PET is not useful in identifying the possible confound of coexisting Lewy pathology.

Indication 3 (Appropriate): Patients with Atypically Young-Onset Dementia

Amyloid PET is appropriate in the scenario in which a relatively young patient (e.g., 50–65 years old, but possibly even younger) presents with a progressive impairment that has features of AD dementia as well as of a non-AD dementia. In the scenario covered by this indication, the dementia specialist is often called on to identify the cause of a devastating illness in such a patient, and to manage a complex and comprehensive evaluation. The purpose of the evaluation is to manage the symptomatic treatment rationally; make appropriate employment, driving, and lifestyle decisions; possibly refer the patient to clinical trials of candidate disease-modifying therapies; and to provide a basis for prognosis and planning for care. The presence or absence of AD pathology in this circumstance is frequently a critical component of the initial differential diagnosis, and it is well known from postmortem studies that clinical diagnosis based on history and examination is often wrong with regard to the presence of AD pathology.

Indication 4 (Not Appropriate): Patients with Core Clinical Criteria for Probable AD with Typical Age of Onset

As mentioned earlier, the AIT identified seven circumstances or scenarios in which amyloid imaging would be inappropriate. The first is indication 4. The AIT recommended against the use of amyloid PET in cases in which core clinical criteria for probable AD dementia were satisfied, and there were typical history and examination findings, because the level of uncertainty would be low and the potential benefit from added information and the potential for altered management would be correspondingly low.

Indication 5 (Not Appropriate): To Determine Dementia Severity

Data are lacking to support the use of amyloid imaging to determine the severity of any cognitive disorder. Thus far, the predominance of the evidence is that the level of A β burden measured with amyloid PET does not correlate well with severity of deficits in patients with dementia.

Indication 5 (Not Appropriate): To Determine Dementia Severity

Data are lacking to support the use of amyloid imaging to determine the severity of any cognitive disorder. Thus far, the predominance of the evidence is that the level of A β burden measured with amyloid PET does not correlate well with severity of deficits in patients with dementia.

Indication 6 (Not Appropriate): Based Solely on a Positive Family History of Dementia or Presence of Apolipoprotein E (APOE) ϵ 4

There are no data currently available that indicate that—based solely on family history or APOE genotype—that prognosis, course, or greater certainty in the cause of cognitive deficits is aided with amyloid PET imaging.

Indication 7 (Not Appropriate): Patients with a Cognitive Complaint That Is Unconfirmed on Clinical Examination

The significance of a cognitive complaint in an elderly person without deficits on examination is currently a topic of active investigation; however, there is insufficient evidence to suggest amyloid PET can aid prognostic judgments or relieve the concerns of such individuals. A negative amyloid PET scan today cannot exclude the possibility of AD dementia in the future.

Indication 8 (Not Appropriate): In Lieu of Genotyping for Suspected Autosomal Mutation Carriers

The use of amyloid PET in lieu of genotyping for suspected autosomal dominant mutation carriers is considered inappropriate. The optimal clinical evaluation in these cases is careful collection of a family history, followed (if appropriate) by genetic counseling prior to and after genetic testing for known mutations. Future use of amyloid PET in autosomal dominant mutation carriers could include determination of whether the amyloid deposition phase of their illness has begun. In the setting of a complete clinical evaluation, including serial neuropsychological testing, this information may be useful in identifying one disease-related milestone that, along with the genetic information, aids decision making.

Indication 9 (Not Appropriate): The Clinical Use of Amyloid PET in Asymptomatic Individuals

The prognostic value of amyloid positivity in normal elderly individuals remains investigational (see the "Further Research Questions" section in the original guideline document). There is a significant potential for patients and families to make inaccurate assumptions about risk and future outcomes on the basis of amyloid PET results. Currently, the potential harms outweigh the minimal benefits. The availability of proven preventative therapies would undoubtedly alter this judgment.

Indication 10 (Not Appropriate): Nonmedical Usage

The AIT did not find any evidence to support the utility of amyloid PET in a context outside of a diagnostic evaluation to determine the cause of cognitive impairment. In particular, no evidence supported a role for amyloid imaging to inform physicians when they are consulted on legal-, disability-, and employment-related matters. These include assessing competency, screening for insurability, or assessing employability or the ability to perform activities of daily living such as driving, piloting an aircraft, or making financial decisions.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Alzheimer's disease (AD)
- Dementia
- Mild cognitive impairment (MCI)

Guideline Category

Diagnosis

Evaluation

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Neurology

Nuclear Medicine

Psychiatry

Radiology

Intended Users

Allied Health Personnel

Hospitals

Physician Assistants

Physicians

Guideline Objective(s)

- To assist in the appropriate use of positron emission tomography (PET) to detect human brain amyloid β (A β) deposition
- To provide health care practitioners with the information necessary to provide their patients with optimal care while also considering the cost-effective use of limited health care resources

Target Population

- Patients with persistent or progressive unexplained mild cognitive impairment (MCI)
- Patients satisfying core clinical criteria for possible Alzheimer's disease (AD) because of unclear clinical presentation, either an atypical clinical course or an etiologically mixed presentation
- Patients with progressive dementia and atypically early age of onset (usually defined as 65 years or less in age)

Interventions and Practices Considered

Amyloid positron emission tomography (PET)

Major Outcomes Considered

- Technical efficacy: analytical validity or technical test performance (i.e., stability, adequacy, and reproducibility of the test itself, including both the image data and the qualitative image interpretation)
- Diagnostic accuracy (clinical validity) based on an autopsy truth standard
- Clinical utility based on a change in management (including change in diagnostic evaluation) and associated improved clinical outcomes

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The Literature Subcommittee used a search strategy as established by the American Academy of Neurology and the National Institutes of Medicine to identify relevant literature. The Amyloid Imaging Taskforce (AIT) deliberated on the choice of literature screening criteria, and a decision was made on the basis of the types of evidence ultimately needed to establish clinical utility of amyloid positron emissions tomography (PET). The ultimate goal was to determine whether there is evidence that using amyloid PET leads to clinically meaningful improvement in outcomes or is useful in medical or personal decision making. Because direct evidence linking amyloid PET to health outcomes is currently lacking, the AIT evaluated existing literature according to a possible chain of evidence consisting of three key questions (refer to the original guideline document for further information on these questions):

- The first question deals with technical efficacy (analytical validity or technical test performance). This class of evidence reflects the stability, adequacy, and reproducibility of the test itself, and includes both the image data and the qualitative image interpretation.
- The second question deals with diagnostic accuracy (clinical validity) based on an autopsy truth standard. As with other elements of validation, each tracer and its associated interpretation protocol must be assessed separately. The AIT elected to include longitudinal clinical studies as ancillary evidence of clinical or diagnostic validity when the design included a baseline amyloid PET followed by clinical evaluation and assessment of longitudinal decline or conversion in clinical status, according to accepted clinical diagnostic criteria.
- The third question deals with clinical utility based on a change in management (including change in diagnostic evaluation) and associated improved clinical outcomes. This is the most challenging component of the analytical framework, and the evidence for a change in clinical management based on amyloid PET is not yet available.

Multiple searches were performed using the National Institutes of Health's PubMed in which 408 publications were initially identified. Literature search limits and parameters were as follows: human, English, and publication date January 01, 2002 to the present. The search terms determined to be the most useful for identifying the pertinent literature were (i) Florbetapir and AV-45, or Amyvid; (ii) PiB or Pittsburgh compound B; (iii) flutemetamol or AV1; (iv) F-18 FDDNP or F18 FDDNP; and (v) florbetaben or 8FBAY94-9172.

Using the PubMed-generated list of 408 documents, the Literature Subcommittee reviewed the list for inclusion and identified a subset of documents by abstract analysis. Documents not relevant to the clinical use of amyloid PET were eliminated based on the primary focus of the reported study and data presented in the document. These include radiochemistry study, in vitro study, animal toxicity study, biodistribution study, image and kinetic analysis study, dosimetry study, pathophysiological investigation, correlational study, study with a small number of subjects, surrogate marker study in therapeutic trials, and review and editorial commentary.

In addition, to ensure appropriate documents were captured during the initial search and review, the AIT performed a backward review to crosscheck the literature included in seminal amyloid imaging reviews with those included in the AIT's initial assessment.

Number of Source Documents

23 documents satisfied the final inclusion criteria.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Not Given)

Rating Scheme for the Strength of the Evidence

Not stated

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

The Literature Subcommittee developed a data extraction form for evidence assessment. The data extraction form included multiple questions and

data extraction sections including whether the document addresses one or more of the potential indications/nonindications proposed by the Indication Subcommittee, individual data points for recalculation of the data, study design, study logistics, patient recruitment setting, inclusion/exclusion criteria, criteria used for diagnosis, inclusion of control subjects, subject characteristics, type of radiopharmaceuticals used, type of positron emission tomography (PET) scanner used, method of PET interpretation and analysis, 2 x 2 data extraction for histopathologically confirmed study as well as mild cognitive impairment to Alzheimer's disease conversion study, a 19-point quality score of the document, the American Academy of Neurology Level of Evidence for a Diagnostic Study Article, the American Academy of Neurology Level of Evidence for a Prognostic Study Article, and whether the document addressed changes in physician confidence.

The Evidence Review Subcommittee conducted evidence assessment in two steps. During the phase I review, valid documents identified during the initial review process were assigned to a pair of reviewers (a dementia specialist and an imaging specialist). Each reviewer scored the documents using the data extraction form. Other documents that met the preliminary inclusion criteria, as indicated by both reviewers, but that received low scores by both reviewers, or mixed scores, or strong reviewer comments for further assessment were also identified as documents to be discussed. During the phase II review, additional documents were identified through the backward review and an updated search, as well as new papers in press. A second round of reviews was conducted identical to phase I. The final inclusion criteria were that the document must contain data of one of two types—either PET–histopathology correlation or PET correlation with longitudinal clinical follow-up. After the review, co-chairs of the AIT reviewed the findings of both phase I and phase II and presented a final list of 23 documents that satisfied the final inclusion criteria and these were presented to the full Amyloid Imaging Taskforce (AIT). These documents were used as the literature-based evidence for rating the appropriate use criteria (AUC) outlined by the Indication Subcommittee.

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

The Amyloid Imaging Taskforce (AIT) formulated appropriate use criteria (AUC) for amyloid positron emission tomography (PET) imaging using procedures similar to those used by groups such as the American College of Cardiology Foundation. The process used (i) identification of potential indications/nonindications, (ii) evidence assessment and rating, (iii) group rating of potential indications/nonindications, (iv) discussion and revoting, and (v) writing. Three AIT subcommittees were established: the Indication Subcommittee, the Literature Subcommittee, and the Evidence Review Subcommittee.

Possible Indications and Nonindications of Clinical Scenarios

The Indication Subcommittee, consisting of practicing dementia specialists and imaging experts, discussed 115 potential indications and nonindications based on multiple clinical and nonclinical scenarios with variables including symptoms, clinical setting, clinical context, evidence of cognitive deficit, family history, knowledge of Alzheimer's disease genetic risk, and age. This process is described below in the "Indications Subcommittee" section. Based on the consensus discussion, the Indication Subcommittee consolidated potential indications and nonindications into 14 scenarios that were subsequently incorporated in a data extraction form used for the evidence assessment.

Rating of the Appropriate Use Criteria

The group rating of potential indications/nonindications was conducted using a rating sheet by individual voting AIT members without knowledge of other members' rating results. Fourteen scenarios proposed by the Indication Subcommittee were consolidated to 10 possible indications/nonindications by defining a preamble that applies to all indications/nonindications. The rating sheet included (i) the final 10 possible indications/nonindications, (ii) the amount of qualified evidence determined by the evidence assessment, and (iii) individual documents that relate to each indication/nonindication. Based on the presented evidence and individual AIT members' opinions, the AIT members were asked to rate each indication/nonindication with Appropriate, Uncertain, or Inappropriate. A nonvoting AIT member summarized the rating results.

Indications Subcommittee

The Expert Work Group consisted of three experienced clinicians, two geriatric cognitive neurologists, and a geriatrician. The developed guidelines for appropriate and inappropriate clinical use are based on available literature as well as expert opinion using a modified Delphi procedure. The first task of the work group was to individually rate appropriateness of 115 different clinical scenarios based on the seven variables listed in Table B1 of the original guideline document. Beginning with the premise that there is value in determining the cause of cognitive impairment, each expert weighed the potential clinical value of amyloid PET against the expense and potential for misuse. After reporting the outcome of these individually considered judgments, the experts came to a consensus about each of the scenarios and used these conclusions to draw generalizations that should

be applicable to many different scenarios.

A second task of the work group was to consider the utility of amyloid PET in eight situations when syndrome classification would be clinically important (e.g., delirium versus dementia) and in 40 clinically relevant differential diagnosis decision points (e.g., Alzheimer's disease vs. frontotemporal dementia). Last, the three clinicians jointly reviewed 10 actual anonymous clinical cases to test whether the guidelines they constructed accurately reflected their own clinical judgment in real rather than strictly theoretical situations. All voting members of the AIT reviewed and discussed the expert-recommended guidelines, and comments were elicited from within and beyond the work group. The final expert guidelines reflect this entire process and are the joint opinion of the entire AIT.

In their deliberations, the AIT assumed that the expert clinician would receive an interpretation of the amyloid PET study as either positive or negative (see the "Definitions" section in the original guideline document). The AIT did not consider the potential impact on the appropriate use criteria of the use of quantitative PET data (i.e., data from automated numerical measurements of specific ligand binding). Currently, there is insufficient published data to recommend a specific implementation of amyloid PET quantitation that could be identified in the appropriate use criteria.

Results of Ratings

Ratings for each indication/nonindication were obtained from independent voting by eight AIT voting members, and the results were summarized by a nonvoting member. At the time of voting, each member was able to access qualified peer-reviewed documents that potentially concern each possible indication, and ratings by AIT members of the quality of the evidence, based on the results of the literature review as described previously. For each indication, the number of supporting publications and the average quality of evidence were indicated on the voting sheet.

Public Commentary

The AIT solicited information from all communities through the Society of Nuclear Medicine and Molecular Imaging and the Alzheimer's Association websites and by direct solicitation to members of these societies. The comments and input helped to shape the development of these appropriate use criteria and the consensus recommendation for the appropriate use of amyloid imaging for clinical indications of the detection of fibrillar amyloid in the brain.

Rating Scheme for the Strength of the Recommendations

Based on the presented evidence and individual Amyloid Imaging Taskforce (AIT) members' opinions, the AIT members were asked to rate each indication/nonindication for the use of amyloid imaging with Appropriate, Uncertain, or Not Appropriate.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

All voting members of the Amyloid Imaging Taskforce (AIT) reviewed and discussed the expert-recommended guidelines, and comments were elicited from within and beyond the work group. The final expert guidelines reflect this entire process and are the joint opinion of the entire AIT.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Incorporating amyloid imaging into clinical decision making may help to narrow a differential diagnosis and simplify some of the complexities inherent in evaluating patients with mild cognitive impairment (MCI) and dementia.
- Although published data concerning amyloid positron emission tomography (PET) results and impact on patient care outcome are extremely limited, amyloid PET is likely to contribute to better patient care under specific circumstances. These are described in the following three domains: change in medication management, change in ordering other tests, and value of knowing. See the original guideline document for further information on these domains.

Potential Harms

- The Amyloid Imaging Taskforce (AIT) considered broader social and psychological implications of amyloid status determination. Although empirical data have not yet been evaluated, the AIT concluded that certain steps should probably be taken by the dementia expert to avoid psychological harm to patients and families that could follow after the initial disclosure of amyloid status. These steps include pretest counseling about the emotional and social implications of both a positive and a negative amyloid positron emission tomography (PET). Implications in the realms of legal and insurance status, including health, life, and long-term care, and employment ramifications are even less well understood at this time, and policymakers should consider whether existing laws such as the Americans With Disabilities Act provide adequate protection for these patients. Notably, the U.S. Genetic Information Nondiscrimination Act applies only to genetic tests.
- A major limitation of amyloid PET to support a diagnosis of Alzheimer's disease (AD) dementia is the high prevalence of amyloid positivity in normal older individuals. Another major caveat is that a positive amyloid scan can also be seen in not only AD, but also in other medical conditions. Refer to the "Limitations of Amyloid PET in Clinical Evaluation" section in the original guideline document for additional discussion.

Qualifying Statements

Qualifying Statements

- As with most guidelines, the health care provider has to make the ultimate judgment regarding the care of each individual patient.
- The health care provider must bear in mind that amyloid imaging does not make a diagnosis of Alzheimer's disease (AD), and by itself does not determine that a patient's cognitive impairment is a result of AD pathology.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Johnson KA, Minoshima S, Bohnen NI, Donohoe KJ, Foster NL, Herscovitch P, Karlawish JH, Rowe CC, Carrillo MC, Hartley DM, Hedrick S, Pappas V, Thies WH. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. J Nucl Med. 2013 Mar;54(3):476-90. [80 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Mar

Guideline Developer(s)

Alzheimer's Association - Disease Specific Society

Society of Nuclear Medicine and Molecular Imaging - Medical Specialty Society

Source(s) of Funding

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) and The Alzheimer's Association

Guideline Committee

Amyloid Imaging Taskforce

Composition of Group That Authored the Guideline

Taskforce Co-chairs: Keith Johnson, MD; Satoshi Minoshima, MD, PhD

Taskforce Voting Members: Nicolaas Bohnen, MD, PhD; Kevin Donohoe, MD; Norman Foster, MD; Peter Herscovitch, MD; Keith Johnson, MD; Jason Karlawish, MD; Satoshi Minoshima, MD, PhD; Christopher Rowe, MD

Scientific Advisor: William Klunk, MD, PhD

Society of Nuclear Medicine and Molecular Imaging (SNMMI) and the Alzheimer's Association (AA) Members: Maria Carrillo, PhD (AA); Dean Hartley, PhD (AA); Saima Hedrick, MPH (SNMMI); Kristi Mitchell MPH (Avalere Health); Virginia Pappas, CAE (SNMMI); William Thies, PhD (AA)

Indication Subcommittee: Norman L. Foster, MD (*Chair*); Jason Karlawish, MD; Christopher Rowe, MD

Literature Subcommittee: Nicolaas Bohnen, MD, PhD (*Chair*); Peter Herscovitch, MD; Kristi Mitchell, MPH

Literature Reviewers: Nicolaas Bohnen, MD PhD; Michael Devous, PhD; Kevin Donohoe, MD; Alex Drezga, MD; Karl Herholz, MD, FRCP; Peter Herscovitch, MD; Keith Johnson, MD; Jason Karlawish, MD; Satoshi Minoshima, MD, PhD; Gil Rabinovici, MD; Christopher Rowe, MD; Victor Villemagne, MD; David Wolk MD

Financial Disclosures/Conflicts of Interest

Relationships with Industry and Management of Conflicts of Interest

The Alzheimer's Association and the Society of Nuclear Medicine and Molecular Imaging rigorously attempted to avoid any actual, perceived, or potential conflicts of interest (COIs) that might have arisen as a result of an outside relationship or personal interest of the writing committee members of the Amyloid Imaging Taskforce (AIT) or of external reviewers used to review specific documents. Both organizations reviewed their own industry relationship policies to ensure that the ensuing process adhered to both standards.

AIT members were required to provide disclosure statements of all relationships that might be perceived as real or potential COIs. These statements were reviewed and discussed by the AIT co-chairs, and were updated and reviewed by an objective third party at the beginning of every AIT meeting and/or teleconference. A table of disclosures for AIT members and external literature reviewers can be found in Table D1 in the original guideline document.

To adjudicate the COIs, the leadership from the Alzheimer's Association and the Society of Nuclear Medicine and Molecular Imaging first determined the threshold for a real COI. After consulting with various experts and reviewing other policies used, the team defined COIs as the following: An individual who has relationships with industry, including consulting, speaking, research, and other nonresearch activities that exceed \$5000 in funding over the previous or upcoming 12-month period.

In addition, if external expert reviewers of the documents were either a principle investigator or other key study personnel on a study, their participation in the review would likely present a COI. All reviewers completed COI forms. Document authors and sponsors were identified and then cross-checked against reviewers' financial and intellectual COIs. Conflicted individuals were noted as unable to review documents in which there was a real COI present.

Of note, William Klunk, MD, co-invented the Pittsburgh compound B-class and Chrysamine-G-class amyloid imaging agents, was appointed as an advisor to the AIT, contributing expertise as requested, but recused himself from any and all discussions that resulted in a vote among writing committee members.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [Society of Nuclear Medicine and Molecular Imaging \(SNMMI\) Web site](#) .

Availability of Companion Documents

The following is available:

- Brain amyloid imaging infographic. Reston (VA): Society of Nuclear Medicine and Molecular Imaging (SNMMI); 2013 May. 1 p.
Electronic copies: Available in Portable Document Format (PDF) from the [Society of Nuclear Medicine and Molecular Imaging \(SNMMI\)](#)
[Web site](#) .

Patient Resources

None available

NGC Status

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